967,605

# PATENT SPECIFICATION

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COMPLETE SPECIFICATION

## Production of Orthodihydroxy Benzene Derivatives

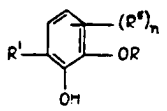
We, MONSANTO COMPANY (formerly known as Monsanto Chemical Company), a corporation organised under the laws of the State of Delaware, United States of America, of 800 North Lindbergh Boulevard, St. Louis, 66, State of Missouri, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to the production of ortho dihydroxy benzene derivatives. More particularly, the invention is concerned with the cleavage of alkyl *o*-hydroxyphenyl ethers in the presence of a tertiary amine and aluminium chloride. The term "cleavage" is used in this specification to refer to the removal of the alkyl group from the ether so that a product is obtained in which the alkyl ether group is converted to an hydroxy group, i.e. the products are ortho dihydroxy benzene derivatives.

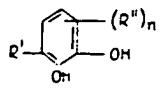
The action of conventional cleavage reagents such as hydrogen chloride, hydrogen bromide, hydrogen iodide, dimethylamine hydrochloride, ethanolamine hydrochloride, pyridine hydrochloride, aluminium chloride and zinc chloride, under vigorous reaction conditions (>100° C.), on alkyl *o*-hydroxyphenyl ethers results in highly-coloured products containing much tar and/or unreacted alkyl *o*-hydroxyphenyl ether. Such products are generally obtained in low yields and are difficult to purify.

It is an object of the present invention to provide an improved method for effecting the cleavage of alkyl-*o*-hydroxyphenyl ethers.

According to the present invention there is provided a process for the production of an ortho dihydroxy benzene derivative of the formula



where R represents a hydrogen atom, $R^1$ represents a hydrogen or halogen atom or an alkyl, alkenyl or alkoxy radical of from 1 to 4 carbon atoms, $R^{11}$ represents a halogen atom or a nitro, sulpho, sulphino, mercapto or hydroxyl group or a hydrocarbon or oxygenated hydrocarbon group containing from 1 to 18 carbon atoms, or an amino methyl, sulphino methyl, mercapto methyl or sulphonyl methyl group and n is 0 or an integer from 1 to 3, which comprises reacting a compound of the said formula but in which R is an alkyl radical of 1 to 4 carbon atoms, with a tertiary amine and anhydrous aluminium chloride in the presence of an inert organic solvent and thereafter hydrolysing the product of such reaction with aqueous acid. The final product is thus a product of the formula



wherein $R^1$, $R^{11}$ and n have the meanings assigned to them above.

As employed in this application, the term "halogen" includes chlorine, bromine, iodine and fluorine. As employed in this application, the term "hydrocarbon radical" includes both the aliphatic and aromatic radicals consisting

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solely of carbon and hydrogen. Illustrative of such hydrocarbon radicals are methyl, ethyl, propyl, isopropyl, *n*-butyl, isobutyl, *sec.*-butyl, *tert.*-butyl, *n*-amyl, isoamyl, *n*-hexyl, isohexyl, heptyl, 2-ethylhexyl, octyl, isooctyl, 2-ethylheptyl, isononyl, decyl, isodecyl, dodecyl, tridecyl, tetradecyl, pentadecyl, octadecyl, cyclobutyl, cyclopentyl, 2-methylcyclopentyl, 3-methylcyclopentyl, 2,4-dimethylcyclopentyl, cyclohexyl, 3,5-dimethylcyclohexyl, cyclohexylmethyl, cyclohexylpropyl, methylcyclohexylethyl, 2-propylcyclohexyl, 3-dodecylcyclohexyl, cycloheptyl, 2,4-dimethylcycloheptyl, 2,3,5-trimethylcycloheptyl, naphthenyl, hydroabietyl, vinyl, allyl, methallyl, propenyl, isopropenyl, 1-butenyl, 2-butenyl, 3-butenyl, pentenyl, hexenyl, heptenyl, octenyl, nonenyl, decenyl, dodecenyl, cyclopentenyl, cyclohexenyl, propargyl, butynyl, octynyl, benzyl, 4-methylbenzyl, 3-caprylbenzyl, phenylethyl, phenylpropyl, phenyldodecyl, phenyl, tolyl, xylyl, cumyl, cymyl, naphthyl, ethylphenyl, xenyl, vinylphenyl and allylphenyl.

As employed in this application, the phrase "oxygenated hydrocarbon radicals" includes not only those radicals wherein a hydrocarbon contains a terminal oxygen atom having a free valence thereon, but also other and different radicals consisting solely of carbon, hydrogen and oxygen wherein the latter forms part of a carbonyl, hydroxyl or alkoxy group. Illustrative of such oxygenated hydrocarbon radicals are methoxy, ethoxy, propoxy, butoxy, pentoxy, octoxy, decoxy, tetradecoxy, hexadecoxy, octadecoxy, cyclopropoxy, cyclobutoxy, cyclohexoxy, methyl cyclopentoxy, cyclohexyl methoxy, cyclohexyl propoxy, cycloheptoxy, 3-dodecyl cyclohexoxy, phenoxy, napththoxy, 3-phenylpropoxy, benzyloxy, 2-phenylethoxy, phenyldecoxy, ethyl phenoxy, toloxy, formyl, carboxy, hydroxymethyl, acetyl, acetoxy, allyloxy, benzoyl and 2,4-dihydroxyphenyl.

As can be seen from preceding illustrations, the substituents represented by $R^{11}$ encompass a very extensive group of radicals. However, the moieties which occupy the meta positions and the para position, in respect to the ortho hydroxy group of the alkyl *o*-hydroxyphenol ether, have not been found to interfere with the desired ether cleavage in any way. The diverse nature of such moieties, particularly in the case of the oxygenated hydrocarbons, will be further exemplified below.

Among the alkyl *o*-hydroxyphenyl ethers which can be cleaved in accordance with this invention are guaiacol, vanillin, isovanillin, acetovanillone, 3-ethoxy-4-hydroxybenzaldehyde, ferualdehyde, syringaldehyde, vanilloyl acetyl, eugenol, chavibetol, isoeugenol, *o*-eugenol, *o*-isoeugenol, isochavibetol, ferulic acid, isoferulic acid, hydroferulic acid, hydroisoferulic acid, hydroxyferulic acid, vanillic acid, isovanillic acid, homovanillic acid, 4-*n*-propyl guaiacol, 5-iodoguaiacol, 5-bromovanillin, 2-nitrovanillin, 6-nitrovanillin, coniferyl alcohol, vanillyl alcohol, vanillyl sulfinic acid, vanillyl amine, vanillyl mercaptan, 4-hydroxy-3-methoxy-5-methylphenyl propane, 4 - hydroxy - 3 - methoxytoluene - w-sulfonic acid, 3,6-dihydroxy-2,4-dimethoxybenzaldehyde, 2-ethoxy - 1 - (4-hydroxy-3-methoxyphenyl) - 1 - propane, 1-(4-hydroxy-3 - methoxyphenyl) - 1,2 - propanedione, 1-ethoxy - 1 - (4 - hydroxy - 3 - methoxyphenyl) - 2 - propanone, 1 - (4 - hydroxy-3-methoxyphenyl) - 2 - propanone, 4 - hydroxy-3 - methoxy - *n* - propylbenzene, 4,4¹-dihydroxy - 3,3¹ - dimethoxystilbene, vanillil, vanilloin, guaiacylacetone, 2,3-dihydroxy-3-guaiacylpropene - 1, 3,4¹,5¹-trimethoxydiphenylmethane, 4-hydroxy-3-methoxytoluene, 2¹,4,4¹ - trihydroxy - 3 - methoxy - 5 - propenylchalcone, 4-hydroxy-3-methoxy ethylbenzyl alcohol and α-guaiacylglycerol.

It should be noted that the cleavage process of this invention is not applicable to ethers which do not conform to the structural formula set forth above. For example, such ethers as veratraldehyde, 3,4-diethoxybenzaldehyde, resorcinol monomethyl ether, *m*-methoxybenzaldehyde and anisole remain virtually unchanged in the presence of the reagents of this invention. It should also be noted that even alkyl *o*-hydroxyphenyl ethers remain virtually unchanged when the other ortho position contains a substituent outside the scope of $R^1$. An example of such a situation is the case of orthovanillin.

Various procedures can be employed in charging of the reactants in the process of this invention. The first procedure consists of slow addition of anhydrous aluminum chloride to the amine while cooling and stirring, followed by addition of the ether and then the solvent. However, this method is somewhat inconvenient since it produces a viscous slurry before addition of the solvent.

Another procedure involves preforming an amine-aluminum chloride complex by adding the amine slowly and with cooling to anhydrous aluminum chloride slurried in a solvent such as pentane. The pentane is distilled off and the remaining solid is added to the ether and the solvent.

A preferred procedure comprises adding a solution of an ether in a solvent to anhydrous aluminum chloride to form a stirrable slurry. The amine is then added slowly and with cooling to complete the charge of reactants. This last procedure has the particular advantage of permitting close control of the temperature during the complex formation because addition of liquids at a uniform rate is much easier than addition of solids and, also, the time required for complex formation is reduced due to dilution of the reactants with the solvent.

Among the tertiary amines which can be used in the present process are the heterocyclic tertiary amines such as pyridine, α-picoline,

γ-picoline, β-picoline, quinoline, isoquinoline, 2-methyl quinoline, 3-methyl quinoline, 4-methyl quinoline, 5-methyl quinoline, 6-methyl quinoline, 7-methyl quinoline, 8-methyl quinoline, 2-ethyl quinoline, 4-ethyl quinoline, 2,3-dimethyl quinoline, 2,4-dimethyl quinoline, 2,8-dimethyl quinoline, 3,4-dimethyl quinoline, 4,6-dimethyl quinoline, 4,7-dimethyl quinoline, 4,8-dimethyl quinoline, 5,8-dimethyl quinoline, 6,8-dimethyl quinoline, 2,3,8-trimethyl quinoline, 2,4,8-trimethyl quinoline, 2-methyl-5-ethyl pyridine, pyrimidine, 2,3-dimethyl pyridine, 2,4-dimethyl pyridine, 2,5-dimethyl pyridine, 2,6-dimethyl pyridine, 3,4-dimethyl pyridine, 3,5-dimethyl pyridine, 2-ethyl pyridine, 3-ethyl pyridine, 4-ethyl pyridine, 2,4,6-trimethyl pyridine, 2-propylpyridine; the aromatic tertiary amines such as N,N-dimethylaniline and N,N-diethylaniline; and the aliphatic tertiary amines such as trimethylamine, triethylamine, tri-*n*-propylamine, triisopropylamine, tri-*n*-butylamine, triisobutylamine, tri-*tert*.-butylamine, triisoamylamine, tri-*n*-amylamine, trihexylamine, diethylmethylamine, dimethylethylamine, dimethylcyclohexylamine, dimethylhexylamine, diethylhexylamine and dimethyldecylamine.

The anhydrous aluminum chloride used in the process of this invention can be prepared by any of a number of methods well known to those skilled in the art. For example, such methods of preparation include chlorination of aluminum metal with chlorine, hydrogen chloride, and metal chlorides, i.e. lead chloride, copper chloride, and silver chloride. Aluminum chloride can also be prepared by the reaction of alumina and aluminiferous ores with chlorine, hydrogen chloride or metal chlorides.

Anhydrous aluminum chloride is extremely hygroscopic and consequently caution should be taken to minimize the exposure of aluminum chloride to the air to avoid premature reaction of said aluminum chloride.

Suitable solvents in which the reaction can be conducted include saturated aliphatic hydrocarbons such as *n*-pentane, iso-pentane, *n*-hexane, 2-methyl pentane, 3-methyl pentane, 2,2-dimethylbutane, 2,3-dimethylbutane and heptane; cycloaliphatic hydrocarbons such as 1,1-dimethyl cyclopropane, 1,1,2-trimethylcyclopropane, 1,2,3-trimethylcyclopropane, cyclobutane, methylcyclobutane, ethylcyclobutane, cyclopentane, methylcyclopentane, methylcyclohexane and cyclohexane; halogenated aliphatic hydrocarbons such as ethyl chloride, ethyl bromide, ethyl iodide, *n*-propyl chloride, isopropyl chloride, butyl chloride, isobutyl chloride, propyl iodide, ethylene dichloride, methylene chloride, methylene bromide, chloroform and carbon tetrachloride; aromatic hydrocarbons such as benzene, toluene, and xylene; halogenated aromatic hydrocarbons such as chlorobenzene, dichlorobenzene, bromobenzene, dibromobenzene, iodobenzene, benzyl chloride, chlorotoluene, bromotoluene and iodotoluene; and nitro derivatives of aromatic hydrocarbons such as nitrobenzene. In general, it is preferred to employ solvents in the process of this invention which are highly polar in nature and are inert under the conditions of the reaction. Solvents which have a boiling point of up to 105° C. are particularly preferred for use in the invention.

The process of the invention is not limited to specific reaction temperatures but may be carried out at temperatures of 0° C. to 105° C. or more. A reaction temperature of 0° C. can be maintained, for example, by employing a cooling bath comprising a slurry of ice in water and using methylene chloride or chloroform as a reaction solvent. The rate of reaction at temperatures 0° C. to 10° C. is, however, somewhat slow. The minimum temperature for the process of this invention is, therefore, the temperature just above that at which no reaction takes place between the alkyl *o*-hydroxyphenyl ether, tertiary amine and aluminium chloride.

Temperatures greater than 105° C. can also be used in the process of this invention. However, at such temperatures, degradation results in considerable tar in the reaction product. At higher temperatures shorter reaction periods may be used to overcome the degradation problem. The yield of product falls off with the longer reaction time at higher temperatures, i.e. greater than 105° C. Temperatures within the range of 0° C. to 55° C. can be most advantageously used, while temperatures within the range of 40° C. to 45° C. are especially preferred.

The tertiary amine, anhydrous aluminium chloride and ether employed in the practice of this invention may be used in widely varying ratios. For example, to each mole of the ether, from 1.4 to 14.0 moles of the amine may be added. Similarly, to each mole of the ether, there may be added from 0.5 to 3.5 moles of the aluminium chloride. A molar ratio of about 4.4 : 1.1 : 1.0 (amine : aluminium chloride : ether) is particularly preferred.

The product of the ether-amine-aluminium chloride reaction is hydrolysed by treatment with an aqueous acid. Although a wide range of acids can be employed for such hydrolysis, it has been found that optimum yields are obtained with acids such as sulphuric, phosphoric and hydrochloric acids.

After the reaction is complete, the product can be recovered by any method known *per se*. However, the process of this invention affords a simple and efficient separation of the reaction product and any unreacted alkyl *o*-hydroxyphenyl ether. Thus, for example, the reaction mixture may be permitted to settle into two phases, i.e. an organic phase and an aqueous phase. It is generally found, upon separation of the two phases, that the aqueous phase contains substantially all of the desired reaction

product, and the organic phase contains any unreacted alkyl *o*-hydroxyphenyl ether. The aqueous phase may be treated by a solvent extraction technique to isolate the desired product. Any unreacted components may be recovered from the organic phase by evaporation for re-use in the process. Alternatively, the organic phase may be dried by azeotropic distillation and recycled to the process.

The following examples will serve to illustrate the invention:—

## Example I

A suitable reaction vessel, designed to exclude atmospheric moisture, is equipped with agitation means, means for measuring the temperature of liquids and vapours, heating and cooling means, and means for condensing vapours. The vessel is charged with 152 grams (1.0 mole) of vanillin and 1500 ml. of methylene chloride, and 146.8 grams (1.1 moles) of anhydrous aluminium chloride is suspended in the charged materials. Pyridine, 348.0 grams (4.4 moles) is then added with agitation and cooling at such a rate as to maintain the reaction temperature at 30—35° C. The resulting solution of the reaction complex in the solvent is heated to the reflux temperature of the solvent (44° C.) and maintained at said temperature for about 24 hours. Said solution is then cooled to 20° C. and hydrolyzed with cooling by the addition of dilute (15—20%) hydrochloric acid until the solution is acidic to a Congo red indicator. The aqueous phase and the methylene chloride phase are separated. The former is extracted with four 500 ml. portions of ether. The combined ether extracts are evaporated to obtain crystalline protocatechualdehyde in a yield of 87% of theory and having a m.p. 153—154° C.

The methylene chloride phase contains substantially all of the unreacted vanillin. Said vanillin may be recovered by evaporation. As an alternative, the methylene chloride phase can be dried by azeotropic distillation and recycled to the process.

## Example II

A reaction vessel as described in Example I is charged with 166 grams (1.0 mole) of acetovanillone and 1500 ml. of methylene chloride, and 146.8 grams (1.1 moles) of anhydrous aluminum chloride is suspended in the charged materials. 348.0 grams (4.4 moles) of pyridine is then added with agitation and cooling at such a rate as to maintain the reaction temperature at 30—35° C. The resulting solution of the reaction complex in the solvent is heated to the reflux temperature of the solvent (44° C.) and maintained at said temperature for about 24 hours. Said solution is then cooled to 20° C. and hydrolyzed with cooling by the addition of dilute (15—20%) hydrochloric acid until the solution is acidic to a Congo red indicator. The aqueous phase and the methylene chloride phase are separated. The former is extracted with four 500 ml. portions of ether. The combined ether extracts are evaporated to obtain crystalline 3,4-dihydroxyacetophenone in a yield of 70% of theory and having a m.p. 110—112° C.

The methylene chloride phase contains substantially all of the unreacted acetovanillone. Said acetovanillone may be recovered by evaporation. As an alternative, the methylene chloride phase can be dried by azeotropic distillation and recycled to the process.

## Example III

Following the procedure of Example I, 124 grams (1.0 mole) of guaiacol, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride and 348.0 grams (4.4 moles) of pyridine are utilized to prepare catechol, m.p. 103—105° C., in a yield of 78% of theory.

## Example IV

Following the procedure of Example I, 152 grams (1.0 mole) of isovanillin, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride and 348 grams (4.4 moles) of pyridine are utilized to prepare protocatechualdehyde, m.p. 153—154° C., in a yield of 88% of theory.

## Examples V—IX

Following the procedure of Example I, 1.0 mole of each of the alkyl *o*-hydroxyphenyl ethers tabulated below is substituted for the vanillin. The product obtained in each instance is as indicated.

| | | |
|---|---|---|
| V. | ether = 2',4,4' - trihydroxy - 3-methoxychalcone | |
| | product = 2',3,4,4' - tetrahydroxychalcone | |
| VI. | ether = 4 - hydroxy - 3 - methoxy ethylbenzyl alcohol | |
| | product = 3,4 - dihydroxy ethylbenzyl alcohol | |
| VII. | ether = 4 - hydroxy - 3 - methoxy dimethylbenzyl alcohol | |
| | product = 3,4 - dihydroxy dimethylbenzyl alcohol | |
| VIII. | ether = 1 - (4 - hydroxy - 3-methoxyphenyl) - 1 - hydroxy - 2-(2-methoxyphenoxy)propane | |
| | product = 1 - (3,4 - dihydroxyphenyl) - 1 - hydroxy - 2-(2-methoxyphenoxy)propane | |
| IX. | ether = syringyl alcohol | |
| | product = 3,4 - dihydroxy - 5-methoxybenzyl alcohol | |

## Example X

A reaction vessel as described in Example I is charged with 152 grams (1.0 mole) of vanillin and 1500 ml. of chloroform, and 146.8 grams (1.1 moles) of anhydrous aluminum

chloride is suspended in the charged materials. 348.0 grams (4.4 moles) of pyridine is then added with agitation and cooling at such a rate as to maintain the reaction temperature at 30—35° C. The resulting solution of the reaction complex in the solvent is heated to the reflux temperature of the solvent (66° C.) and maintained at said temperature for about 24 hours. Said solution is then cooled to 20° C. and hydrolyzed with cooling by the addition of dilute (15—20%) hydrochloric acid until the solution is acidic to a Congo red indicator. The aqueous phase and the chloroform phase are separated. The former is extracted with four 500 ml. portions of ether. The combined ether extracts are evaporated to obtain crystalline protocatechualdehyde in a yield of 77% of theory and having a m.p. 153—154° C.

The chloroform phase contains substantially all of the unreacted vanillin. Said vanillin may be recovered by evaporation. As an alternative the chloroform phase can be dried by azeotropic distillation and recycled to the process.

## Example XI

A reaction vessel as described in Example I is charged with 152 grams (1.0 mole) of vanillin and 1500 ml. of chloroform, and 146.8 grams (1.1 moles) of anhydrous aluminum chloride is suspended in the charged materials. 348.0 grams (4.4 moles) of pyridine is then added with agitation and cooling at such a rate as to maintain the reaction temperature at 30—35° C. The resulting solution of the reaction complex in the solvent is heated to a temperature of 45° C. and maintained at said temperature for about 24 hours. Said solution is then cooled to 20° C. and hydrolyzed with cooling by the addition of dilute (15—20%) hydrochloric acid until the solution is acidic to a Congo red indicator. The aqueous phase and the chloroform phase are separated. The former is extracted with four 500 ml. portions of ether. The combined ether extracts are evaporated to obtain crystalline protocatechualdehyde in a yield of 76% of theory and having a m.p. 152—153° C.

The chloroform phase contains substantially all of the unreacted vanillin. Said vanillin may be recovered by evaporation. As an alternative, the chloroform phase can be dried by azeotropic distillation and recycled to the process.

## Example XII

A reaction vessel as described in Example I is charged with 152 grams (1.0 mole) of vanillin and 1500 ml. of ethyl bromide, and 146.8 grams (1.1 moles) of anhydrous aluminum chloride is suspended in the charged materials. 348.0 grams (4.4 moles) of pyridine is then added with agitation and cooling at such a rate as to maintain the reaction temperature at 30—35° C. The resulting solution of the reaction complex in the solvent is heated to the reflux temperature of the solvent (40° C.) and maintained at said temperature for about 24 hours. Said solution is then cooled to 20° C. and hydrolyzed with cooling by the addition of dilute (15—20%) hydrochloric acid until the solution is acidic to a Congo red indicator. The aqueous phase and the ethyl bromide phase are separated. The former is extracted with four 500 ml. portions of ether. The combined ether extracts are evaporated to obtain crystalline protocatechualdehyde in a yield of 87% of theory and having a m.p. 153—154° C.

The ethyl bromide phase contains substantially all of the unreacted vanillin. Said vanillin may be recovered by evaporation. As an alternative, the ethyl bromide phase can be dried by azeotropic distillation and recycled to the process.

## Example XIII

Following the procedure of Example I, 182 grams (1.0 mole) of syringaldehyde, 146.8 grams (1.1 mole) of anhydrous aluminum chloride, 1500 ml. of methylene chloride and 348.0 grams (4.4 moles) of pyridine are utilized to prepare 3-methoxy-4,5-dihydroxybenzaldehyde, m.p. 131—133° C., in a yield of 79% of theory.

## Example XIV

A reaction vessel as described in Example I is charged with 152 grams (1.0 mole) of vanillin and 1500 ml. of ethylene dichloride, and 146.8 gram (1.1 moles) of anhydrous aluminum chloride is suspended in the charged materials. 348.0 gram (4.4 moles) of pyridine is then added with agitation and cooling at such a rate as to maintain the reaction temperature at 30—35° C. The resulting solution of the reaction complex in the solvent is heated to a temperature of 45° C. and maintained at said temperature for about 24 hours. Said solution is then cooled to 20° C. and hydrolyzed with cooling by the addition of dilute (15—20%) hydrochloric acid until the solution is acidic to a Congo red indicator. The aqueous phase and the ethylene dichloride phase are separated. The former is extracted with four 500 ml. portions of ether. The combined ether extracts are evaporated to obtain crystalline protocatechualdehyde in a yield of 76% of theory and having a m.p. 149—151° C.

The ethylene dichloride phase contains substantially all of the unreacted vanillin. Said vanillin may be recovered by evaporation. As an alternative, the ethylene dichloride phase can be dried by azeotropic distillation and recycled to the process.

## Example XV

Following the procedure of Example I, 152 grams (1.0 mole) of vanillin, 146.8 grams

(1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 410 grams (4.4 moles) of γ-picoline are utilized to prepare protocatechualdehyde in a yield of 73% of theory.

EXAMPLE XVI

Following the procedure of Example I, 152 grams (1.0 mole) of vanillin, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 410 grams (4.4 moles) of α-picoline were utilized to prepare protocatechualdehyde in a yield of 41% of theory.

EXAMPLE XVII

Following the procedure of Example I, 152 grams (1.0 mole) of vanillin, 146.8 grams (1.1 moles) of anhydrous aluminum chloride 1500 ml. of methylene chloride, and 567 grams (4.4 moles) of quinoline are utilized to prepare protocatechualdehyde in a yield of 23% of theory.

EXAMPLE XVIII

Following the procedure of Example I, 152 grams (1.0 mole) of vanillin, 146.8 grams (1.1 moles) of anhydrous aluminum chloride 1500 ml. of methylene chloride and 532 grams (4.4 moles) of N,N-dimethylaniline are utilized to prepare protocatechualdehyde in a yield of 33% of theory.

EXAMPLE XIX

A reaction vessel as described in Example I is charged with 166 grams (1.0 mole) of 3 - ethoxy - 4 - hydroxybenzaldehyde and 1500 ml. of methylene chloride, and 146.8 grams (1.1 moles) of anhydrous aluminum chloride is suspended in the charged materials. 348.0 grams (4.4 moles) of pyridine is then added with agitation and cooling at such a rate as to maintain the reaction temperature at 30—35° C. The resulting solution of the reaction complex in the solvent is heated to the reflux temperature of the solvent (44° C.) and maintained at said temperature for about 48 hours. Said solution is then cooled to 20° C. and hydrolyzed with cooling by the addition of dilute (15—20%) hydrochloric acid until the solution is acidic to a Congo red indicator. The aqueous phase and the methylene chloride phase are separated. The former is extracted with four 500 ml. portions of ether. The combined ether extracts are evaporated to obtain crystalline protocatechualdehyde in a yield of 32% of theory.

The methylene chloride phase contains substantially all of the unreacted 3-ethoxy-4-hydroxybenzaldehyde. Said 3-ethoxy-4-hydroxybenzaldehyde may be recovered by evaporation. As an alternative, the methylene chloride phase can be dried by azeotropic distillation and recycled to the process.

EXAMPLES XX—XXIII

Following the procedure of Example I, 1.0 mole of each of the alkyl *o*-hydroxyphenyl ethers tabulated below is substituted for the benzaldehyde. The product obtained in each instance is as indicated.

XX. ether = β-hydroxyconiferyl alcohol
product = 3 - (3,4 - dihydroxyphenyl) - 2 - propen - 1,2-diol

XXI. ether = 4 - hydroxy - 3 - methoxybenzyl alcohol
product = 3,4 - dihydroxybenzyl alcohol

XXII. ether = β - hydroxypropionylguaiacone
product = 2,3',4' - trihydroxypropiophenone

XXIII. ether = coniferyl aldehyde
product = 3,4 - dihydroxycinnamaldehyde

EXAMPLE XXIV

Following the procedure of Example I, 168 grams (1.0 mole) of vanillic acid, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 348 grams (4.4 moles) of pyridine are utilized to prepare protocatechuic acid in a yield of 28% of theory.

EXAMPLE XXV

Following the procedure of Example I, 152.0 grams (1.0 mole) of vanillin, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride and 444 grams (4.4 moles) of triethylamine are utilized to prepare protocatechualdehyde, m.p. 152—154° C., in a yield of 62% of theory.

EXAMPLE XXVI

Following the procedure of Example I, 231 grams (1.0 mole) of 5-bromovanillin, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 348 grams (4.4 moles) of pyridine are utilized to prepare 5-bromo-protocatechualdehyde, m.p. 225—227° C., in a yield of 90% of theory.

EXAMPLE XXVII

Following the procedure of Example I, 164 grams (1.0 mole) of eugenol, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 348 grams (4.4 moles) of pyridine are utilized to prepare 4-allyl catechol, m.p. 48—50° C., in good yield.

EXAMPLE XXVIII

Following the procedure of Example I, 197 grams (1.0 mole) of 2-nitrovanillin, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 348 grams (4.4 moles) of pyridine are utilized to prepare 2-nitroprotocatechualdehyde in excellent yield.

EXAMPLE XXIX

Following the procedure of Example I, 153 grams (1.0 mole) of vanillyl amine, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 348 grams (4.4 moles) of pyridine are utilized to prepare 3,4-dihydroxybenzylamine in good yield.

EXAMPLE XXX

Following the procedure of Example I, 186 grams (1.0 mole) of vanillyl sulfinic acid, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 348 grams (4.4 moles) of pyridine are utilized to prepare 3,4-dihydroxybenzyl sulfinic acid in a high yield.

EXAMPLE XXXI

Following the procedure of Example I, 170 grams (1.0 mole) of vanillyl mercaptan, 146.8 grams (1.1 moles) of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 348 grams (4.4 moles) of pyridine are utilized to prepare 3,4-dihydroxybenzyl mercaptan in good yield.

EXAMPLE XXXII

Following the procedure of Example I, 218 grams (1.0 mole) of 4-hydroxy-3-methoxytoluene - w - sulfonic acid, 146.8 grams (1.1 moles of anhydrous aluminum chloride, 1500 ml. of methylene chloride, and 348 grams (4.4 moles) of pyridine are utilized to prepare 3,4-dihydroxytoluene - w - sulfonic acid in a high yield.

The following table represents additional examples of the present invention, wherein the apparatus of Example I is utilized and the procedure and reactants employed are as specified.

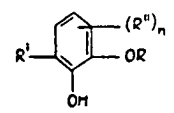
TABLE I

| Example No. | Molar Ratios Reactants Pyridine : $AlCl_3$ : Vanillin | Solvent | Reaction Temp. °C. | Reaction Time-hrs. | % Conversion |
|---|---|---|---|---|---|
| XXXIII | 3.5 : 3.5 : 1 | Hexane | 68 | 1 | 34.1 |
| XXXIV | 14 : 3.5 : 1 | $CHCl_3$ | 0—10 | 48 | 16.8 |
| XXXV | 18.9 : 3.5 : 1 | $CHCl_3$ | 25—30 | 24 | 38.5 |
| XXXVI | 9.2 : 2.3 : 1 | $CHCl_3$ | 25—30 | 24 | 66.7 |
| XXXVII | 4.4 : 1.1 : 1 | $CHCl_3$ | 25—30 | 72 | 68.1 |
| XXXVIII | 2.2 : 0.55 : 1 | $CHCl_3$ | 40—45 | 24 | 51.5 |
| XXXIX | 2.2 : 0.55 : 1 | $CHCl_3$ | 50—55 | 24 | 52.8 |
| XXXX | 1.4 : 0.35 : 1 | $CHCl_3$ | 50—55 | 24 | 37 |
| XXXXI | 4.4 : 1.1 : 1 | $C_6H_5NO_2$ | 25—30 | 24 | 33.8 |
| XXXXII | 14 : 3.5 : 1 | $CHCl_3$ | 40—45 | 24 | 73.4 |
| XXXXIII | 4.4 : 1.1 : 1 | $CHCl_3$ | 40—45 | 24 | 75.4 |

From these exemplary preparations it will be seen that this invention provides a simple and inexpensive method for cleaving alkyl *o*-hydroxyphenyl ethers. The reaction conditions are mild, and a pure product is recovered with comparative ease.

WHAT WE CLAIM IS:—

1. A process for the production of an ortho dihydroxy benzene derivative of the formula:




where R is a hydrogen atom, $R^1$ represents a hydrogen or halogen atom or an alkyl, alkenyl

or alkoxy radical containing from 1 to 4 carbon atoms. $R^{11}$ represents a halogen atom or a nitro, sulpho, sulphino, mercapto or hydroxyl group or a hydrocarbon or oxygenated hydrocarbon group, containing from 1 to 18 carbon atoms or amino methyl, sulphino methyl, mercapto methyl, or sulphonyl methyl group, and n is 0 or an integer from 1 to 3, which comprises reacting a compound of the said formula but in which R is an alkyl radical of 1 to 4 carbon atoms, with a tertiary amine and anhydrous aluminium chloride in the presence of an inert organic solvent, and thereafter hydrolysing the product of said reaction with aqueous acid.

2. A process according to claim 1 wherein the tertiary amine employed is a heterocyclic tertiary amine.

3. A process according to claim 2 wherein the heterocylic tertiary amine is pyridine.

4. A process according to claim 2 wherein the heterocyclic tertiary amine is γ-picoline.

5. A process according to claim 1 wherein the tertiary amine employed is an aliphatic tertiary amine.

6. A process according to claim 5 wherein the aliphatic tertiary amine is triethylamine.

7. A process according to any of claims 1—6 wherein the inert organic solvent is methylene chloride.

8. A process of preparing catechol which comprises reacting guaiacol according to the process described in claim 1.

9. A process of preparing protocatechualdehyde which comprises reacting vanillin according to the process claimed in claim 1.

10. A process of preparing 3,4-dihydroxyacetophenone which comprises reacting acetovanillone according to the process claimed in claim 1.

11. A process of preparing 3,4-dihydroxy-5-methoxy-benzaldehyde which comprises reacting syringaldehyde according to the process claimed in claim 1.

12. A process of preparing 5-bromoprotocatechualdehyde which comprises reacting 5-bromovanillin according to the process claimed in claim 1.

13. A process according to any of claims 8—12 wherein the tertiary amine is pyridine and the inert organic solvent is methylene chloride.

14. A process according to claim 1 substantially as hereinbefore described with reference to any of the foregoing specific examples I to XXXXIII.

15. Ortho dihydroxy benzene derivatives whenever prepared or produced by any of the processes hereinbefore described and claimed.

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